



PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 53836

Title: Diagnostic challenges in non cirrhotic portal hypertension

Reviewer's code: 05078668

Position: Peer Reviewer

Academic degree: MD

Professional title: Associate Professor

Reviewer's Country/Territory: India

Author's Country/Territory: Romania

Manuscript submission date: 2019-12-30

Reviewer chosen by: Jin-Zhou Tang

Reviewer accepted review: 2020-01-11 10:23

Reviewer performed review: 2020-01-16 15:21

Review time: 5 Days and 4 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No



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SPECIFIC COMMENTS TO AUTHORS

Authors have titled the manuscript as NCPHT. But they have discussed the new entity of PSDV. Hence the title is not appropriate to the content. Are the authors interested in highlighting vascular liver disorders that cause portal hypertension? Some aspects of the manuscript are not agreeable 1)1st para: Budd chiari syndrome can be classically categorised as NCPHT as late stages of BCS can progress to cirrhosis (post sinusoidal cause of cirrhosis) 2)2nd para: Commonly EHPVO is not difficult to diagnosis from cirrhosis. A portal cavernoma on imaging differentiates the two. In rare cases (10%) a cirrhosis may have a portal vein thrombosis due to abnormal coagulation or concomitant HCC. Conversely <5% of EHPVO may progress to behave like cirrhosis or be complicated by secondary biliary cirrhosis in symptomatic cholangiopathy (10%) 3)The word "Imagistic examination" throughout the text is not clear 4)Authors should clarify PSDV vs "cryptogenic cirrhosis" and PSDV vs "non-cirrhotic portal fibrosis" (with references to pediatric/young population) 5)Remove the entity on VOD..not pertinent to this review 6)Spelling and grammatical errors need attention 7) Table 2 endoscopy finding comparison is not impressive. 8) comment on splenic vein status in the entities described with respect to EHPVO and NCPF



PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 53836

Title: Diagnostic challenges in non cirrhotic portal hypertension

Reviewer's code: 01426451

Position: Editorial Board

Academic degree: MD, PhD

Professional title: Professor

Reviewer's Country/Territory: Denmark

Author's Country/Territory: Romania

Manuscript submission date: 2019-12-30

Reviewer chosen by: Jin-Zhou Tang

Reviewer accepted review: 2020-01-12 14:30

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Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input type="checkbox"/> Anonymous <input checked="" type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No



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SPECIFIC COMMENTS TO AUTHORS

In general, this manuscript is well written and reviews an important area with some new definitions and clinical handling of a difficult patient group I have a few specific comments, please see below. In addition, I think there need a section on treatment of complications in this patient group or discussion on the use of terlipressin for variceal bleeding, betablockers as prophylaxis, ascites etc. Diagnostic sections are relevant and well described bu need a few references, see below

Comments: Regarding hemodynamic investigations the measurement of spleen pressure should be mentioned and two important publications cited. Combined liver vein and spleen pulp pressure measurements in patients with portal or splenic vein thrombosis. Keiding S, et al Scand J Gastroenterol. 2004 Jun;39(6):594-9. PMID:15223686; β -Blockers Improve Presinusoidal Portal Hypertension. Sørensen M, et al. Dig Dis Sci. 2018 Nov;63(11):3153-3157. doi: 10.1007/s10620-018-5186-1. Epub 2018 Jul 12. PMID: 30003386. They showed that the gradient may be estimated as shown in the first paper and that beta-blockers may reduce this gradient

Minor comments: Page 2, line 1: "the prognostic is relatively good, in the case of cirrhosis the outcome is completely different." Prognostic changed to prognosis Page 2, 2nd paragraph: It should be noted that ascites develops after a trigger factor, and is usually transient[1],[2]. May develop? Prefer imaging in opposition to imagistic, please change throughout the manuscript table 2: "predominat vascular" should be predominant



PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

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Title: Diagnostic challenges in non cirrhotic portal hypertension

Reviewer's code: 04761926

Position: Peer Reviewer

Academic degree: PhD

Professional title: Doctor

Reviewer's Country/Territory: Italy

Author's Country/Territory: Romania

Manuscript submission date: 2019-12-30

Reviewer chosen by: AI Technique

Reviewer accepted review: 2020-01-01 15:24

Reviewer performed review: 2020-01-18 15:24

Review time: 17 Days

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input checked="" type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No



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SPECIFIC COMMENTS TO AUTHORS

The authors present a very clear and exhaustive review on non-cirrhotic portal hypertension and report data in line with the most updated guidelines on the management of vascular liver disease. In particular they underline the difficulty of suspect and diagnose PSVD and the more difficulty challenge to differentiate between PSVD and other liver disease such as compensated cirrhosis, chronic portal vein thrombosis, SOS, or healthy population that may share different aspects/characteristics of the disease. The paper is well written and well argued, I have only few comments: 1. Title: it reflects the major contents of the article, and is comparable to the aim of the work. 2. Core tip: ok 3. Introduction: ok 4.1. Differentiation between PSVD and hepatic cirrhosis: please correct "hepatic cirrhosis" simply in "cirrhosis" 4.2. Differentiation between PSVD and EHPVO: ok 4.3. Differentiation between PSDV and healthy population: -In this section the authors correctly mention the case of patients with OPV at histology but without portal hypertension that now are contemplated in the last definition of PSVD. Due to the absence of clinical signs of portal hypertension such as splenomegaly, esophageal varices, thrombocytopenia etc., it results very difficult to suspect the presence of PSVD. However, as described in literature, most of patients with OPV have not normal liver tests. In fact, the principal indication to realize a liver biopsy is the presence of elevated transaminases or cholestasis with no evident causes. The authors are invited to mention concept that is an important and useful data to differentiate PSVD and healthy population. 4.4. PSVD and Sinusoidal obstruction syndrome: The mechanism which whom this drugs toxic to vascular liver system and in particular oxaliplatin and azathioprine is not well understood. As the authors state is probably related to the depletion of glutathione transferase leading to toxic insult to sinusoidal endothelial cells. However, the description of the mechanism of NRH provided to the authors ("obstruction is caused by erythrocytes sloughing, and blebs,



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characterized by free fragments of cytoplasmic processes, occasionally containing cellular organelle") seems to correspond more properly to the pathogenetic mechanism of SOS, not of NRH/PSVD. Please verify and modify the abovementioned statement. 5. Illustrations and tables: ok 6. Biostatistics: not required. 7. Units: ok 8. References: ok 9. Quality of manuscript organization and presentation: please correct the typo "PSDV" in "PSVD" in the title of the paragraph "Differentiation between PSDV and healthy population". 10. Ethics statements: not required.



PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 53836

Title: Diagnostic challenges in non cirrhotic portal hypertension

Reviewer's code: 02527808

Position: Editor-in-Chief

Academic degree: MD

Professional title: Professor

Reviewer's Country/Territory: Egypt

Author's Country/Territory: Romania

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Reviewer chosen by: Jin-Zhou Tang

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Review time: 7 Days and 1 Hour

Scientific quality	<input checked="" type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input checked="" type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
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SPECIFIC COMMENTS TO AUTHORS

Well written manuscript covering most of the important challenges in the diagnosis of NCPH and their difficult differentiation from cirrhotics -some minor comments : - A Table listed all causes of NCPH is important and needed some points of differentiation like immunohistochemistry is mentioned in the table only while not mentioned in the text